

## Letter to the Editor

# Increasing rate of hospitalizations for food-induced anaphylaxis in Italian children: An analysis of the Italian Ministry of Health database

To the Editor:

The clinical pattern of food allergy (FA) in childhood is changing in many Western countries. The most severe clinical manifestation of FA is anaphylaxis. The number of food-induced anaphylaxis (FIA) cases seems to be increasing in the United States and Australia.<sup>1,2</sup> Few studies of FIA in European children have been conducted in recent years, and most were limited by small populations or a regional focus.<sup>3-5</sup>

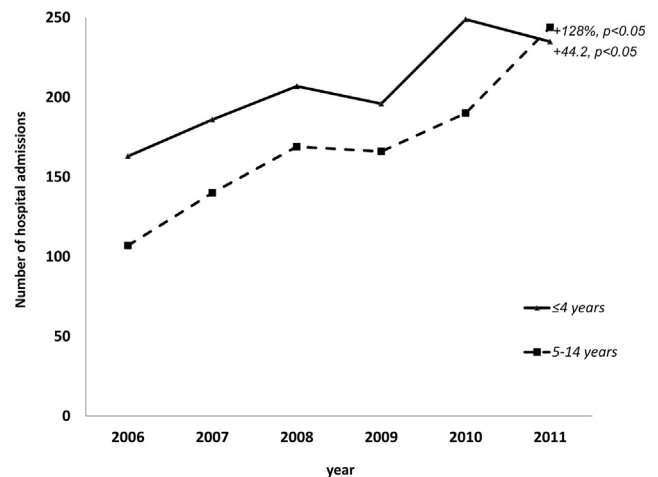
We previously reported an alarming increasing trend in hospital admissions for FIA among Italian children during the 2001 to 2005 period.<sup>6</sup> To explore whether this trend has continued during more recent years, we investigated with a retrospective, case-based study the number of FIA-related hospital admissions and the food responsible for the episode in children 14 years or younger living in Italy by querying the statistics system database of the Italian Ministry of Health (<http://www.salute.gov.it>) in all Italian hospitals between January 1, 2006, and December 31, 2011, using the *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) discharge diagnostic codes for FIA. The number of fatal cases of FIA was also recorded. Data regarding the Italian pediatric population living in those years were from the Italian National Institute of Statistics database (<http://www.istat.it>). See this article's Online Repository at [www.jacionline.org](http://www.jacionline.org) for a description of data collection.

A total of 3121 FIA-related hospital admissions of 2552 subjects (mean age, 15.5 years; minimum, 0 year; maximum, 92 years; 56.5% males) were identified with the ICD-9-CM codes during the 6-year study period. Hospital admissions for FIA occurred mainly in the North of Italy (2253, 72.2%;  $P < .01$ ). During the same period, there were 2252 FIA-related admissions (72.1%) of 1785 patients 14 years or younger (mean age, 5.18 years; 60.9% boys). In these patients also, FIA-related hospital admissions occurred mainly in the North of Italy (1724, 76.5%;  $P < .01$ ).

When examining FIA hospitalization rates by age, we observed that the increased incidence of hospital admissions for FIA was more pronounced in children aged 5 to 14 years than in those younger than 4 years (+128% and +44.2%, respectively;  $P < .05$ ) (Fig 1). An increasing trend of the number of hospital admissions for FIA for patients older than 14 years was also found (+63.8%;  $P < .05$ ), with a rise in all age groups. Four fatal cases of FIA were identified in patients older than 14 years, and the foods responsible were peanuts, crustaceans, fruits, and vegetables; in 1 case, the food responsible was not reported.

Fig 2 shows the rate of FIA episodes according to the ICD-9-CM code and age group ( $\leq 4$  years and 5-14 years). A total of 17.2% of the subjects 14 years or younger required multiple hospital admissions for FIA (from 2 to 10 times per year) in the same year. In most cases, children were younger than 4 years (67.8%) (see Fig E1 in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)).

Considering the pediatric population aged 14 years or younger living in Italy during the 6-year study period (ranging from



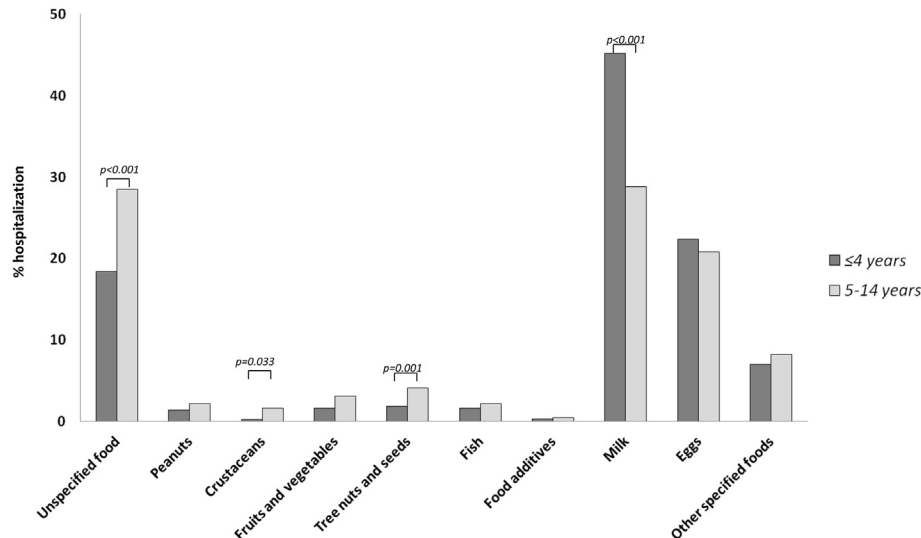
**FIG 1.** Increasing trend of the number of hospital admissions for FIA among Italian children from 2006 to 2011. The increased incidence of hospital admissions for FIA was more pronounced in children aged 5 to 14 years than in those younger than 4 years (+128% and +44.2%, respectively;  $P < .05$ ).

8,337,511 in 2006 to 8,380,158 in 2011), we estimate an incidence of hospital admission for FIA of about 4.4 episodes per 100,000 children/year. Given our previous results related to the 2001 to 2006 period,<sup>6</sup> and the Italian pediatric population 14 years or younger between 2001 and 2011, we estimate that the rate of hospital admissions for FIA among the Italian pediatric population increased from about 0.001% in 2001 to 0.005% in 2011 ( $P < .05$ ) (see Fig E2 in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org)).

Our results demonstrate a continuous increasing trend in the hospital admission rate for FIA in Italian children. It appears that every 23 hours a child in Italy requires hospital admission because of FIA.

This increase could be related to several factors. One could be the general increase in FA prevalence among children and the increased susceptibility to many allergens. The North-South gradient observed in our study, which is in line with results obtained in Australia and the United States,<sup>7,8</sup> suggests a potential role for vitamin D insufficiency. It has been reported that decreased sunlight/ultraviolet B exposure contributes to immune system defects, abnormal gut microbiota, gastrointestinal infections, and compromised mucosal barrier integrity, leading to sensitization and FA.<sup>7,8</sup> According to this view, a high prevalence of vitamin D deficiency was identified in Italian children (>50% of the subjects), most of whom lived in Northern Italy (average latitude of 45 degrees).<sup>9</sup>

A strength of our study is that we queried a nationwide hospital and vital statistics database. This study design is particularly useful in time trends because clinical practice and principal discharge diagnosis coding are unlikely to change significantly during a relatively short period. The main limitation of our study is related to the possibility of inaccurate coding and that individual anaphylaxis cases are not validated by medical record review. Unexpectedly, a relatively high percentage of children 4 years or younger (17.2%) required multiple hospital admissions for FIA in



**FIG 2.** Main foods responsible for anaphylaxis requiring hospitalization among Italian children as reported by the specific ICD-9-CM code.

the same year (from 2 to 10 times per year). In most cases, the children were younger than 4 years (67.8%).

In conclusion, FIA-related hospital admissions in Italian children increased year on year from 2001 to 2011. This finding suggests that the trend is also increasing in the European pediatric population as well as in the United States and Australia. This alarming finding should prompt (1) studies aimed at identifying the causative factor(s), (2) policies to ensure safe environments for children affected by FA, and (3) more effective health care strategies to limit the burden of FA and to prevent FIA hospitalizations.

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## DESCRIPTION OF DATA COLLECTION

Through a specific application we queried the episode statistics system database of the Italian Ministry of Health for FIA-related hospital admissions in all subjects presenting to all public hospitals in Italy between January 1, 2006, and December 31, 2011 (the last year for which data were available in the database at the time of the analysis) using the ICD-9-CM discharge diagnostic codes for FIA: 995.60, anaphylactic shock caused by unspecified food; 995.61, anaphylactic shock caused by peanuts; 995.62, anaphylactic shock caused by crustaceans; 995.63, anaphylactic shock caused by fruits and vegetables; 995.64, anaphylactic shock caused by tree nuts and seeds; 995.65, anaphylactic shock caused by fish; 995.66, anaphylactic shock caused by food additives; 995.67, anaphylactic shock caused by milk product; 995.68, anaphylactic shock caused by eggs; and 995.69, anaphylactic shock caused by other specified food.

This is the only data set on hospital use, outcomes, and charges designed to study children's use of hospital services in Italy.

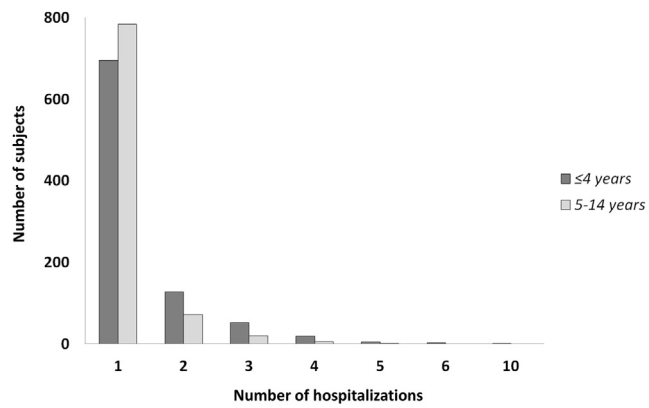
Database contains discharge-level records, not patient-level records. The target in our population includes pediatric and adult discharges from community, and the discharges are sorted by patient's age, sex, year and location of the admitting hospital, and the number of fatal cases. Although the hospital database has changed during the study period (ie, the number of Italian hospitals), the changes would not appear to have significantly affected the findings of increased FIA-related hospital admissions observed.

Access to database is limited to a specific request. Uses are limited to research and statistical reporting.

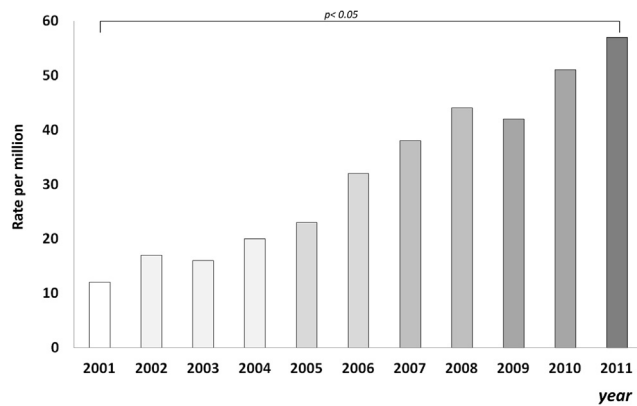
For more information on the database, visit the Italian Ministry of Health Web site at <http://www.salute.gov.it>.

## REFERENCE

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**FIG E1.** Recurrence of hospitalization in the same patient for FIA in a single year.



**FIG E2.** Trend in admission rate for FIA in Italian pediatric population (subjects aged  $\leq 14$  years) between 2001 and 2011. The data from 2001 to 2005 are from Berni Canani et al.<sup>E1</sup>